a.) Amendment to the Specification

Please amend the paragraph starting at page 33, line 30 and ending at page 34, line 3 to read as follows.

(102) The thiazole derivative according to the above (101), wherein R^{4B} is lower alkyl, aralkyl or aromatic ~~heterocyclic-aralkyl,~~ heterocyclic-alkyl, or a pharmaceutically acceptable salt thereof.

Please amend the paragraphs starting at page 40, line 4 and ending at page 41, line 11 to read as follows.

(x) Examples of the alicyclic heterocyclic moiety of the alicyclic heterocyclic group, the alicyclic heterocyclic-alkyl and the alicyclic heterocyclic-methyl include 3-membered to 6-membered monocyclic alicyclic heterocyclic groups containing at least one atom selected from a nitrogen atom, an oxygen atom and a sulfur atom; or bicyclic or tricyclic condensed-ring alicyclic heterocyclic groups containing at least one atom selected from a nitrogen atom, an oxygen atom and a sulfur atom in which 4- to 8-membered rings are condensed; such as pyrrolidinyl, imidazolidinyl, thiazolidinyl, piperidinyl, piperazinyl, morpholinyl, thiomorpholinyl, piperidino, morpholino, thiomorpholino, oxazolinyl, dioxolanyl, dioxanyl, dioxepanyl, dihydropyridyl, tetrahydropyridyl, pyranyl, dihydropyranyl, tetrahydropyranyl, tetrahydroisoquinolinyl, tetrahydroquinolinyl, indolinyl, isoindolinyl, ~~octahydropyrazino[2,1-c][1,4]oxazinyl,~~ dihydropyridazinyl, oxiranyl, oxetanyl, oxolanyl, thiolanyl, thianyl, aziridinyl, azetidinyl, azolidinyl, perhydroxazepinyl, perhydrothiazepinyl, perhydroazepinyl, perhydroazocinyl, perhydrodiazepinyl, succinimido, phthalimido, glutarimido, 1,3-benzodioxolyl, 1,4-

benzodioxanyl, 3,4-dihydro-2H-1,5-benzodioxepinyl, 1,4-dioxaspiro[4.5]decanyl, 1,4-dioxa-8-azaspiro[4.5]decanyl, octahydropyrrolo[1,2-a]pyrazinyl, octahydropyrazino[2,1-c][1,4]oxazinyl and octahydropyrazino[2,1-c][1,4]thiazinyl.

(xi) Examples of the alicyclic heterocyclic group containing at least one oxygen atom include the alicyclic heterocyclic groups containing at least one oxygen atom described in the above examples of the alicyclic heterocyclic group (x), such as morpholinyl, morpholino, oxazolinyl, dioxolanyl, dioxanyl, dioxepanyl, pyranyl, dihydropyranyl, tetrahydropyranyl, ~~octahydropyrazino[2,1-c][1,4]oxazinyl,~~ oxiranyl, oxetanyl, oxolanyl, perhydroxazepinyl, 1,3-benzodioxolyl, 1,4-benzodioxanyl, 3,4-dihydro-2H-1,5-benzodioxepinyl, 1,4-dioxaspiro[4.5]decanyl, 1,4-dioxa-8-azaspiro[4.5]decanyl and octahydropyrazino[2,1-c][1,4]oxazinyl.

Please amend the paragraph at page 64, lines 17-23 to read as follows.

Examples of the base include pyridine, triethylamine, ~~diisopropylamine,~~ diisopropylethylamine, DBU, DMAP, N-methylmorpholine, N-methylpiperidine, potassium acetate, potassium carbonate, cesium carbonate, sodium carbonate, sodium hydrogencarbonate, sodium hydroxide, lithium hydroxide, potassium hydroxide and potassium phosphate. These may be used herein either singly in a combination of two or more.

Please amend the paragraph at page 72, lines 17-21 to read as follows.

Compound (Im) can be produced by reacting Compound (Ik) with 1 to 100 equivalents of ~~$R^{8a}CHO$~~ $R^{8c}CHO$ in an inert solvent to the reaction in the presence of 1 to 20 equivalents of a base at a temperature between -78°C and room temperature for 5 minutes to 48 hours.

Please amend the paragraph at page 160, lines 6-7 to read as follows.

~~N-[4-(2-Furyl)-5-(4-pyridyl)thiazol-2-yl]-(3-pyridyl)acetamide~~ N-[4-(2-Furyl)-5-(4-pyridyl)thiazol-2-yl]-2-(3-pyridyl)acetamide (Compound 13)

Please amend the paragraph at page 173, lines 19-26 to read as follows.

Methyl 6-chloromethylnicotinate (1.30 g, 7.00 mmol) obtained according to the method described in WO02/92455 was added to 2 mol/L hydrochloric acid, followed by stirring under heating and reflux for 5 hours. The reaction mixture was allowed to cool down to room temperature, and the precipitated solid was collected by filtration to afford ~~6-chloromethylnicotinic~~ 6-(chloromethyl)nicotinic acid (539 mg, 45 %).

Please amend the paragraph at page 174, lines 1-15 to read as follows.

~~6-Chloromethylnicotinic~~ 6-(Chloromethyl)nicotinic acid (172 mg, 1.00 mmol) obtained in Step 1, 2-amino-4-(2-furyl)-5-morpholinothiazole (251 mg, 1.00 mmol) obtained in Step 1 of Example 29 and PyBOP (572 mg, 1.10 mmol) were dissolved in

DMF (4 mL), and triethylamine (0.307 mL, 2.20 mmol) was added thereto, followed by stirring at room temperature for 2 hours. The reaction mixture was poured into water, followed by extraction with ethyl acetate. The organic layer was washed with a saturated aqueous solution of sodium chloride and dried over anhydrous magnesium sulfate, and then the solvent was distilled away under the reduced pressure. The resulting residue was purified through silica gel column chromatography (hexane:ethyl acetate = 2:1 to 1:3) to afford the entitled Compound 36 (194 mg, 48 %).

Please amend the paragraph starting at page 175, line 30 and ending at page 176, line 14 to read as follows.

2-Chloroisonicotinic acid (5.00 g, 31.7 mmol) was added to thionyl chloride (40 mL), followed by stirring under heating and reflux for 2 hours. The reaction mixture was concentrated under reduced pressure, and the resulting residue was dissolved in dichloromethane (1 mL). The resulting solution was added to a pyridine (16 mL) solution of 2-amino-4-(2-furyl)-5-morpholinothiazole (880 mg, 5.00 mmol) obtained in Step 1 of Example 29, and then N,N-dimethylaminopyridine (~~48.8 mmol~~ 48.8 mg, 0.400 mmol) was added thereto, followed by stirring at room temperature for 1 hour. The reaction mixture was concentrated under reduced pressure, and the resulting residue was purified through silica gel column chromatography (hexane:ethyl acetate = 1:3 to ethyl acetate) to afford the entitled Compound 39 (1.05 g, 66 %)

Please amend the paragraph at page 184, lines 20-22 to read as follows.

~~1-(6-Chloro-3-pyridazinyl)-N-[4-(2-furyl)-5-morpholinothiazol-2-yl]piperidine-4-carboxamide~~ 1-(6-Chloropyridazin-3-yl)-N-[4-(2-furyl)-5-morpholinothiazol-2-yl]piperidine-4-carboxamide (Compound 53)

Please amend the paragraph at page 187, lines 28-29 to read as follows.

~~N-[4-(2-Furyl)-5-morpholinothiazol-2-yl]-1-morpholinocarbonylpiperidine-4-carboxamide~~ N-[4-(2-Furyl)-5-morpholinothiazol-2-yl]-1-(morpholinocarbonyl)piperidine-4-carboxamide (Compound 56)

Please amend the paragraphs starting at page 189, line 14 and ending at page 190, line 5 to read as follows.

~~4-Bromomethyl-N-[4-(2-furyl)-5-morpholinothiazol-2-yl]benzamide~~ 4-(Bromomethyl)-N-[4-(2-furyl)-5-(morpholinothiazol-2-yl]benzamide (Compound 59)

~~4-Bromomethylbenzoic~~ 4-(Bromomethyl)benzoic acid (2.24 g, 10.4 mmol) was dissolved in toluene (80 mL), and thionyl chloride (7.59 mL, 104 mmol) was added thereto, followed by stirring under heating and reflux for 6 hours. The reaction mixture was concentrated under reduced pressure. The resulting residue was dissolved in THF (50 mL), and 2-amino-4-(2-furyl)-5-morpholinothiazole (2.00 g, 7.97 mmol) obtained in Step 1 of Example 29, triethylamine (1.67 mL, 12.0 mmol) and N,N-dimethylaminopyridine (97.6 mg, 0.800 mmol) were added thereto, followed by stirring under heating and reflux for 1 hour. The reaction mixture was allowed to cool down to room temperature, and then

a 10 % aqueous solution of sodium carbonate was added thereto, followed by extraction with ethyl acetate. The organic layer was washed with a saturated aqueous solution of sodium chloride and dried over anhydrous magnesium sulfate, and then the solvent was distilled away under reduced pressure. The resulting residue was purified through silica gel column chromatography (chloroform:ethyl acetate = 9:1) to afford the entitled Compound 59 (3.29 g, 92 %).

Please amend the paragraph at page 191, lines 2-3 to read as follows.

~~N-[4-(2-Furyl)-5-morpholinothiazol-2-yl]-4-(4-hydroxypiperidinomethyl)benzamide~~ N-[4-(2-Furyl)-5-morpholinothiazol-2-yl]-4-[4-(hydroxypiperidino)methyl]benzamide (Compound 61)

Please amend the paragraph starting at page 191, line 30 and ending at page 192, line 1 to read as follows.

~~N-[4-(2-Furyl)-5-morpholinothiazol-2-yl]-4-[N-(2-methoxyethyl)-N-methylaminomethyl]benzamide~~ N-[4-(2-Furyl)-5-morpholinothiazol-2-yl]-4-{[N-(2-methoxyethyl)-N-methylamino]methyl}benzamide (Compound 63)

Please amend the paragraphs starting at page 192, line 15 and ending at page 194 line 17 to read as follows.

~~N-[4-(2-Furyl)-5-morpholinothiazol-2-yl]-4-(2-oxopiperidinomethyl)benzamide~~ N-[4-(2-Furyl)-5-morpholinothiazol-2-yl]-4-[2-(oxopiperidino)methyl]benzamide (Compound 64)

Step 1:

60 % sodium hydride (600 mg, 15.0 mmol) was suspended in DMF (30 mL), 2-piperidone (1.49 g, 15.0 mmol) was added thereto, followed by stirring at room temperature for 30 minutes. A solution of methyl 4-bromomethylbenzoate (2.29 g, 10.0 mmol) in DMF (10 mL) was added to the reaction mixture, followed by stirring at room temperature for 3 hours. The reaction mixture was poured into a saturated aqueous solution of sodium chloride, followed by extraction with ethyl acetate. The organic layer was dried over anhydrous magnesium sulfate, and then the solvent was distilled away under reduced pressure. The resulting residue was purified through silica gel column chromatography (ethyl acetate:methanol = 9:1) to afford methyl ~~4-(2-oxopiperidinomethyl)benzoate~~ 4-[(2-oxopiperidino)methyl]benzoate (2.47 g 100 %).

^{1}H NMR ($CDCl_3$, δ ppm): 1.74-1.85 (m, 4H), 2.46-2.51 (m, 2H), 3.20-3.22 (m, 2H), 3.91 (s, 3H), 4.64 (s, 2H), 7.31 (d, J = 8.0 Hz, 2H), 8.00 (d, J = 8.0 Hz, 2H).

Step 2:

Methyl ~~4-(2-oxopiperidinomethyl)benzoate~~ 4-[(2-oxopiperidino)methyl]benzoate (2.47 g, 10.0 mmol) obtained in Step 1 was dissolved in a mixed solvent of methanol (30 mL) and water (10 mL), and lithium hydroxide monohydrate (2.10 g, 50.0 mmol) was added thereto, followed by stirring at room temperature for 30 minutes. The reaction mixture was concentrated under reduced pressure, and 6 mol/L hydrochloric acid was added to the resulting residue to adjust the pH to 1, followed by extraction with chloroform. The organic layer was dried over anhydrous magnesium sulfate, and then the solvent was distilled away under reduced pressure to

afford ~~4-(2-oxopiperidinomethyl)benzoic~~ 4-[(2-oxopiperidino)methyl]benzoic acid (629 mg. 27 %).

^{1}H NMR (DMSO-d_6, δ ppm): 1.69-1.75 (m, 4H), 2.27-2.34 (m, 2H), 3.14-3.22 (m, 2H), 4.56 (s, 2H), 7.31 (d, J = 8.4 Hz, 2H), 7.90 (d, J = 8.4 Hz, 2H).

Step 3:

~~4-(2-Oxopiperidinomethyl)benzoic~~ 4-[(2-Oxopiperidino)methyl]benzoic acid (233 mg, 1.00 mmol) obtained in Step 2 was dissolved in dichloromethane (10 mL), and thionyl chloride (5 mL) was added thereto, followed by stirring under heating and reflux for 1 hour. The reaction mixture was concentrated under reduced pressure, and the resulting residue was dissolved in chloroform (5 mL). The resulting solution was added to a solution of 2-amino-4-(2-furyl)-5-morpholinothiazole (126 mg, 0.50 mmol) in pyridine (10 mL) obtained in Step 1 of Example 29, followed by stirring at room temperature for 1 hour. The reaction mixture was concentrated under reduced pressure, and the resulting residue was purified through silica gel column chromatography (chloroform:methanol = 20:1) to afford the entitled Compound 64 (68.3 mg, 29 %).

^{1}H NMR ($CDCl_3$, δ ppm): 1.81-1.84 (m, 4H), 2.48-2.51 (m, 2H), 3.03 (t, J = 4.6 Hz, 4H), 3.22-3.26 (m, 2H), 3.90 (t, J = 4.6 Hz, 4H), 4.66 (s, 2H), 6.51 (dd, J = 1.9, 3.5 Hz, 1H), 6.88 (dd, J = 0.5, 3.5 Hz, 1H), 7.45 (dd, J = 0.5, 1.9 Hz, 1H), 7.67 (d, J = 13.5 Hz, 2H), 7.87 (d, J = 13.5 Hz, 2H), 9.45 (br s, 1H).

APCIMS m/z: $[M+H]^+$ 467.

[Example 65]

~~N-[4-(2-Furyl)-5-morpholinothiazol-2-yl]-4-(2-oxo-1,2-dihydropyridin-1-ylmethyl)benzamide~~ N-[4-(2-Furyl)-5-morpholinothiazol-2-yl]-4-[(2-oxo-1,2-dihydropyridin-1-yl)methyl]benzamide (Compound 65)

Please amend the paragraphs starting at page 211, line 11 and ending at page 212, line 11 to read as follows.

~~N-[4-(2-Furyl)-5-(morpholinomethyl)thiazol-2-yl]-3-pyridinecarboxamide~~ N-[4-(2-Furyl)-5-(morpholinomethyl)thiazol-2-yl] pyridine-3-carboxamide (Compound 94)

Compound 93 (1.15 g, 0.32 mmol) was dissolved in trifluoroacetic acid (12 mL), followed by stirring at room temperature for 30 minutes. The reaction mixture was concentrated under reduced pressure, and aqueous 1 mol/L sodium hydroxide solution and a mixed solvent (4:1) of chloroform and 2-propanol were added to the resulting residue, and the organic layer was separated. The organic layer was dried over anhydrous magnesium sulfate, and then the solvent was distilled away under reduced pressure to afford ~~2-amino-4-(2-furyl)-5-morpholinomethylthiazole~~ 2-amino-4-(2-furyl)-5-(morpholinomethyl)thiazole (835 mg, 100 %).

^{1}H NMR (CD_3OD, δ ppm): 2.50-2.53 (m, 4H), 3.65-3.68 (m, 4H), 3.83 (s, 2H), 6.47 (dd, J = 1.8, 3.3 Hz, 1H), 6.61 (dd, J = 0.7, 3.3 Hz, 1H), 7.52 (dd, J = 0.7, 1.8 Hz, 1H).

Step 2:

~~2-Amino-4-(2-furyl)-5-morpholinomethylthiazole~~ 2-Amino-4-(2-furyl)-5-(morpholinomethyl)thiazole (225 mg, 0.85 mmol) obtained in Step 1 was dissolved in DMF (4 mL), and nicotinoyl chloride hydrochloride (302 mg, 1.70 mmol) and

triethylamine (0.24 mL, 1.70 mmol) were added thereto, followed by stirring at room temperature for 4 hours. A saturated aqueous solution of sodium hydrogencarbonate was added to the reaction mixture, followed by extraction with ethyl acetate. The organic layer was dried over anhydrous magnesium sulfate, and then the solvent was distilled away under reduced pressure. The resulting residue was purified through silica gel column chromatography (hexane:ethyl acetate = 1:1) to afford the entitled Compound 94 (73.0 mg, 23 %).

Please amend the paragraph at page 221, lines 9-12 to read as follows.

In a manner similar to that in Example 108, by using 4-hydroxypiperidine in place of imidazole, the entitled Compound 111 (92.0 mg, 53 %) was obtained from Compound 107 (150 mg, 0.387 mmol).

Please amend the paragraph starting at page 223, line 22 and ending at page 224, line 10 to read as follows.

Compound n (300 mg, 0.760 mmol) obtained in Reference Example 14, tributyl(2-furyl)stannane (0.720 mL, 2.28 mmol), silver oxide (0.180 g, 0.760 mmol) and tetrakis(triphenylphosphine)palladium (0.130 g, 0.114 mmol) were suspended in DMF (7.6 mL), followed by stirring at 60°C for 2 hours and at 100°C for 15 minutes. The reaction mixture was cooled with ice, ethyl acetate was added thereto, and the precipitated silver oxide was collected by filtration. The filtrate was concentrated under reduced pressure. A 10 % aqueous solution (35 mL) of potassium fluoride was added to the resulting residue,

followed by stirring at room temperature for 10 minutes, and then extracted with ethyl acetate. The organic layer was washed with a saturated aqueous solution of sodium chloride and dried over anhydrous magnesium sulfate, and then the solvent was distilled away under reduced pressure. The resulting residue was purified through silica gel column chromatography (hexane:ethyl acetate = 10:1 to 5:1) to afford the entitled ~~Compound 114~~ Compound 115 (20.6 mg, 8 %).

Please amend the paragraph at page 224, lines 20-24 to read as follows.

In a manner similar to that in Example 115, by using tributyl(2-thienyl)stannane (0.240 mL, 0.750 mmol) in place of tributyl(2-furyl)stannane, the entitled ~~Compound 115~~ Compound 116 (98.9 mg, 100 %) was obtained from Compound n (100 mg, 0.250 mmol) obtained in Reference Example 14.

Please amend the paragraph at page 229, lines 13-18 to read as follows.

In a manner similar to that in Step 1 of Example 123, by using ethyl iodide in place of methyl iodide, 2-amino-5-(1-ethyl-2-oxo-1,2-dihydropyridin-4-yl)-4-(2-furyl)thiazole ~~(0.185 mg, 3.00 mmol)~~ (167 mg, 58%) was obtained from Compound p (259 mg, 1.00 mmol) obtained in Reference Example 16.

Please amend the paragraph at page 232, lines 10-21 to read as follows.

2-Amino-4-(2-furyl)-5-(1-methyl-2-oxo-1,2-dihydropyridin-5-yl)thiazole (200 mg, 0.732 mmol) obtained in Step 1 was dissolved in DMF (4 mL), and isonicotinic acid (180 mg, 1.46 mmol), PyBOP (838 mg, 1.61 mmol) and triethylamine (0.449 mL, 3.21 mmol) were added thereto, followed by stirring at 80°C for 1 hour. The reaction mixture was poured into water, and the precipitated solid was collected by filtration. The resulting solid was purified through silica gel column chromatography (chloroform:methanol = 17:1), followed by reslurrying with methanol to afford the entitled ~~Compound 111~~ Compound 126 (155 mg, 56 %) as a pale yellow solid.

Please amend the paragraph at page 238, lines 1-5 to read as follows.

In a manner similar to that in Example 96, by using ~~N,O-dimethylhydroxyamine~~ N,O-dimethylhydroxylamine hydrochloride in place of morpholine, the entitled Compound 134 (2.59 g, 49 %) was obtained from Compound 133 (4.65 g, 15.0 mmol), in place of Compound 95.

Please amend the paragraphs at page 242, lines 8-14 to read as follows.

~~2-Chloromethyl-N-[5-benzoyl-4-(2-furyl)thiazol-2-yl]pyridine-4-carboxamide~~ 2-(Chloromethyl)-N-[5-benzoyl-4-(2-furyl)thiazol-2-yl]pyridine-4-carboxamide (Compound 140)

In a manner similar to that in Example 137, by using ~~2-chloromethylisonicotinic~~ 2-(chloromethy)lisonicotinic acid obtained according to the

method described in WO03/043636 in place of 2-hydroxy-2-methylpropanoic acid, the entitled Compound 140 (712 mg, 91 %) was obtained from Compound 136 (500 mg, 1.85 mmol).

Please amend the paragraph at page 247, lines 3-4 to read as follows.

N-[5-Benzoyl-4-(2-furyl)thiazol-2-yl]-2-oxo-1,2-dihydropyridine-5-carboxamide ~~(Compound 147)~~ (Compound 149)

Please amend the paragraph at page 249, lines 10-13 to read as follows.

In a manner similar to that in Example 137, by using pyridazine-4-carboxylic acid in place of ~~2-hydroxy-2-propanoic~~ 2-hydroxy-2-methylpropanoic acid, the entitled Compound 153 (154 mg, 74 %) was obtained from Compound 136 (150 mg, 0.555 mmol).

Please amend the paragraph at page 258, lines 10-14 to read as follows.

In a manner similar to that in Example 154, by using 2-chlorobenzoyl chloride in place of 2-methylbenzoyl chloride, the entitled ~~Compound 166~~ Compound 171 (290 mg, 48 %) was obtained from Compound h (520 mg, 1.51 mmol) obtained in Reference Example 8.

Please amend the paragraph starting at page 264, line 30 and ending at page 265, line 5 to read as follows.

In a manner similar to that in Example 3, by using isonicotinic acid in place of methoxyacetic acid, followed by reslurrying with a mixed solvent of ethanol and diethyl ether, the entitled ~~Compound 181~~ Compound 184 (130 mg, 77 %) was obtained from Compound 183 (129 mg, 0.438 mmol) in place of Compound a.

Please amend the paragraph at page 265, lines 16-30 to read as follows.

Picolinic acid (1.00 g, 8.12 mmol) was dissolved in DMF (40 mL), and N,O-dimethylhydroxylamine hydrochloride (1.58 g, 16.2 mmol), EDC hydrochloride (3.12 g, 16.2 mmol), 1-hydroxybenzotriazole monohydrate ~~(2.48 mg, 16.2 mmol)~~ (2.48 g, 16.2 mmol) and triethylamine (2.25 ml, 16.2 mmol) were added thereto, followed by stirring at 50°C for 3 hours. A saturated aqueous solution of sodium hydrogencarbonate was added to the reaction mixture, followed by extraction with ethyl acetate. The organic layer was washed with a saturated aqueous solution of sodium chloride and dried over anhydrous magnesium sulfate, and then the solvent was distilled away under reduced pressure. The resulting residue was purified through silica gel column chromatography (hexane:ethyl acetate = 1:4) to afford N-methoxy-N-methylpyridine-2-carboxamide (988 mg, 73 %).

Please amend the paragraph at page 281, lines 13-25 to read as follows.

Compound 186 (600 mg, 2.22 mmol) was dissolved in DMF (11 mL), and Compound 1 ~~(1.43 mg, 5.53 mmol)~~ (1.43 g, 5.53 mmol) obtained in Reference Example 12,

N,N-diisopropylethylamine (2.34 mL, 13.3 mmol) and PyBOP (4.03 g, 7.74 mmol) were added thereto, followed by stirring at 50°C for 10 hours. Water was added to the reaction mixture, followed by extraction with ethyl acetate. The organic layer was washed with a saturated aqueous solution of sodium chloride and dried over anhydrous magnesium sulfate, and then the solvent was distilled away under reduced pressure. The resulting residue was purified through silica gel column chromatography to afford the entitled Compound 213 (912 mg, 81 %) as a pale yellow oily substance.

Please amend the paragraph at page 297, lines 19-23 to read as follows.

In a manner similar to that in Example 188, by using 5-isoxazolecarbonyl chloride ~~(0.240 mg, 1.89 mmol)~~ (240 mg, 1.89 mmol) in place of acetyl chloride, the entitled Compound 242 (333 mg, 82 %) was obtained as a brown solid from Compound 186 (300 mg, 1.11 mmol).

Please amend the paragraph at page 305, lines 6-22 to read as follows.

Compound 186 (100 mg, 0.369 mmol) was suspended in dichloromethane (3.7 mL), and carbonyldiimidazole ~~(89.7 mg, 554 mmol)~~ (89.7 mg, 0.554 mmol) was added thereto at room temperature, followed by stirring for 12 hours at room temperature. The reaction mixture was concentrated under reduced pressure, and the resulting residue was dissolved in THF (3.7 mL). Morpholine ~~(0.0484 mL, 554 mmol)~~ (0.0484 mL, 0.554 mmol) was added to the resulting solution, followed by stirring for 2 hours at room temperature. Water was added to the reaction mixture, followed by extraction with ethyl

acetate. The organic layer was washed with a saturated aqueous solution of sodium chloride and dried over anhydrous magnesium sulfate, and then the solvent was distilled away under reduced pressure. The resulting residue was purified through silica gel column chromatography (chloroform:methanol = 20:1) to afford the entitled Compound 256 (93.9 mg, 66 %) as a pale yellow solid.

Please amend the paragraph at page 306, lines 4-16 to read as follows.

Compound y (130 mg, 0.437 mmol) obtained in Reference Example 25 was suspended in THF (4.4 mL), and piperidine ~~(64.9 mL, 0.656 mmol)~~ (64.9 μL, 0.656 mmol) was added thereto, followed by stirring at room temperature for 20 hours. Water was added to the reaction mixture, followed by extraction with ethyl acetate. The organic layer was washed with a saturated aqueous solution of sodium chloride and dried over anhydrous magnesium sulfate, and then the solvent was distilled away under reduced pressure. The resulting residue was purified through silica gel column chromatography (hexane:ethyl acetate = 1:1) to afford the entitled Compound 257 (66.5 mg, 40 %) as a pale yellow solid.

Please amend the paragraph at page 311, lines 8-9 to read as follows.

N-[4-(2-Furyl)-5-(pyridin-2-ylcarbonyl)thiazol-2-yl]-2-(4-methylpiperidino)acetamide ~~(Compound 276)~~ (Compound 266)

Please amend the paragraph at page 324, lines 16-24 to read as follows.

In a manner similar to that in Example 287, by using 1-ethylpiperazine in place of morpholine, a free form of the entitled ~~Compound 289~~ Compound 290 was obtained from Compound 286 (100 mg, 0.350 mmol). The resulting free form was dissolved in acetone (3 mL), and a 4 mol/L solution of hydrogen chloride (0.263 mL, 1.05 mmol) in ethyl acetate was added thereto. The precipitated solid was collected by filtration to afford the entitled Compound 290 (89.0 mg, 49 %).

Please amend the paragraph at page 327, lines 11-13 to read as follows.

~~tert-Butyl N-[4-(2-furyl)-5-[1-hydroxy-1-(5-methoxypyridin-2-yl)methyl]thiazol-2-yl]carbamate~~ tert-Butyl N-{4-(2-furyl)-5-[1-hydroxy-1-(5-methoxypyridin-2-yl)methyl]thiazol-2-yl}carbamate (Compound 296)

Please amend the paragraph at page 329, lines 7-22 to read as follows.

A THF solution (10 mL) of 2,6-dibromopyridine (4.97 g, 21.0 mmol) was added to a 2.0 mol/L solution of isopropylmagnesium chloride in THF ~~(9.56 mL, 10.1 mmol)~~ (9.56 mL, 19.1 mmol) at 0°C, followed by stirring for 3 hours at room temperature. A THF solution (5 mL) of Compound 98 (1.37 g, 3.82 mmol) was added dropwise to the reaction mixture, followed by stirring for 3 hours at room temperature. The reaction mixture was poured into a saturated aqueous solution of ammonium chloride, followed by extraction with ethyl acetate. The organic layer was washed with a saturated aqueous solution of sodium chloride and dried over anhydrous magnesium sulfate, and then the

solvent was distilled away under reduced pressure. The resulting residue was purified through silica gel column chromatography (chloroform:methanol = 9:1) to afford the entitled Compound 300 (520 mg, 31 %).

Please amend the paragraph at page 332, lines 19-23 to read as follows.

In a manner similar to that in Example 188, by using 2-furoyl chloride ~~(75.5 mL, 0.766 mmol)~~ (75.5 μL, 0.766 mmol) in place of acetyl chloride, the entitled Compound 307 (20.7 mg, 13 %) was obtained from Compound 303 (116 mg, 0.428 mmol) in place of Compound 186.

Please amend the paragraph at page 339, lines 22-23 to read as follows.

2-Amino-4-(2-furyl)thiazol-5-yl 2-chloropyridin-5-yl ketone ~~(Compound 322)~~ (Compound 321)

Please amend the paragraph at page 348, lines 20-21 to read as follows.

~~tert-Butyl N-[4-(furan-2-yl)-5-(furan-2-ylcarbonyl)thiazol-2-yl]carbamate~~ tert-Butyl N-[4-(2-furyl)-5-(furan-2-ylcarbonyl)thiazol-2-yl]carbamate (Compound 340)

Please amend the paragraphs at page 349, lines 1-10 to read as follows.

~~2-Amino-4-(4-furan-2-yl)thiazol-5-yl furan-2-yl ketone~~ 2-Amino-4-(2-furyl)thiazol-5-yl 2-furyl ketone (Compound 341)

In a manner similar to that in Example 186, the entitled Compound 341 (115 mg, 85 %) was obtained from Compound 340 (187 mg, 0.519 mmol) in place of Compound 185.

^{1}H NMR ($CDCl_3$, δ ppm): 6.45-6.46 (m, 1H), 6.49-6.51 (m, 1H), 7.17-7.18 (m, 1H), 7.40-7.44 (m, 2H), 7.51-7.52 (m, 1H).

[Example 342]

~~N-[4-(Furan-2-yl)-5-(furan-2-ylcarbonyl)thiazol-2-yl]pyridine-4-carboxamide~~ N-[4-(2-Furyl)-5-(furan-2-ylcarbonyl)thiazol-2-yl]pyridine-4-carboxamide (Compound 342)

Please amend the paragraphs at page 350, lines 6-28 to read as follows.

~~tert-Butyl N-[4-(furan-2-yl)-5-(furan-3-ylcarbonyl)thiazol-2-yl]carbamate~~ tert-Butyl N-[4-(2-furyl)-5-(furan-3-ylcarbonyl)thiazol-2-yl]carbamate (Compound 344)

In a manner similar to that in Example 185, by using 3-furancarboxylic acid in place of picolinic acid, the entitled Compound 344 (79.0 mg, 15 %) was obtained from Compound h (500 mg, 1.45 mmol) obtained in Reference Example 8.

^{1}H NMR ($CDCl_3$, δppm): 1.50 (s, 9H), 6.44-6.48 (m, 1H), 6.82-6.83 (m, 1H), 7.31-7.45 (m, 3H), 7.94-7.96 (m, 1H), 8.67 (br s, 1H).

[Example 345]

~~2-Amino-4-(2-furyl)thiazol-5-yl furan-3-yl~~ 2-Amino-4-(2-furyl)thiazol-5-yl 3-furyl ketone (Compound 345)

In a manner similar to that in Example 186, the entitled Compound 345 (40.0 mg, 70 %) was obtained from Compound 344 (79.0 mg, 0.219 mmol) in place of Compound 185.

^{1}H NMR ($CDCl_3$, δ ppm): 6.39 (dd, J = 1.8, 3.7 Hz, 1H), 6.67 (dd, J = 0.7, 1.8 Hz, 1H), 7.21 (dd, J = 0.7, 3.7 Hz, 1H), 7.32-7.33 (m, 1H), 7.34-7.35 (m, 1H), 7.78-7.79 (m, 1H).

[Example 346]

~~N-[4-(Furan-2-yl)-5-(furan-3-ylcarbonyl)thiazol-2-yl]pyridine-4-carboxamide~~ N-[4-(2-furyl)-5-(furan-3-ylcarbonyl)thiazol-2-yl]pyridine-4-carboxamide (Compound 346)

Please amend the paragraph at page 377, lines 22-23 to read as follows.

tert-Butyl N-[4-(2-furyl)-5-pivaloylthiazol-2-yl]carbamate ~~(Compound 403)~~ (Compound 398)

Please amend the paragraph at page 389, lines 28-29 to read as follows.

N-[5-(Cyclobutylcarbonyl)-4-(2-furyl)thiazol-2-yl]pyridine-4-carboxamide ~~(Compound 442)~~ (Compound 424)

Please amend the paragraph at page 399, lines 15-18 to read as follows.

In a manner similar to that in Example 442, by using 4-cyanobenzoic acid in place of isonicotinic acid, the entitled Compound 443 (199 mg, 62 %) was obtained from Compound 441 (226 mg, 0.738 mmol).

Please amend the paragraph at page 420, lines 3-14 to read as follows.

Compound 454 (125 mg, 0.450 mmol) and DMAP ~~(0.022 mmol)~~ (2.69 mg, 0.022 mmol) were suspended in pyridine (2 mL), and 2-(trifluoromethoxy)benzoyl chloride (202 mg, 0.900 mmol) was added thereto, followed by stirring at 80°C for 6 hours. The reaction mixture was poured into water, followed by extraction with ethyl acetate. The organic layer was washed with a saturated aqueous solution of sodium chloride and dried over anhydrous magnesium sulfate, and then the solvent was distilled away under reduced pressure. The resulting residue was recrystallized from ethanol to afford the entitled Compound 475 (111 mg, 53 %) as a pale yellow solid.

Please amend the paragraph starting at page 421, line 26 and ending at page 422, line 11 to read as follows.

4-(Chloromethyl)benzoyl chloride (942 mg, 4.99 mmol) was dissolved in THF (16 mL), and Compound 454 (1.11 g, 3.99 mmol), triethylamine (0.840 mL, 5.98 mmol) and DMAP (50.0 mg, 0.400 mmol) were added thereto, followed by stirring under heating and reflux for 2 hours. The reaction mixture was concentrated under reduced pressure, and water was added to the resulting residue, followed by extraction with

chloroform. The organic layer was washed successively with a saturated aqueous solution of sodium hydrogencarbonate and a saturated aqueous solution of sodium chloride and dried over anhydrous magnesium sulfate, and then the solvent was distilled away under reduced pressure. The resulting residue was purified through silica gel column chromatography (chloroform:methanol = 99:1), followed by reslurrying with methanol to afford the entitled ~~Compound 476~~ Compound 478 (1.42 g, 83 %) as an ocher solid.

Please amend the paragraph at page 423, lines 12-20 to read as follows.

Compound 478 (340 mg, 0.789 mmol) was suspended in THF (3 mL), and piperidine ~~(0.390 mmol, 3.95 mmol)~~ (0.390 ml, 3.95 mmol) was added thereto, followed by stirring under heating and reflux for 1.5 hours. The solvent was distilled away under reduced pressure, and the resulting residue was purified through silica gel column chromatography (chloroform:methanol = 4:1), followed by reslurrying with diethyl ether to afford the entitled Compound 480 (262 mg, 69 %) as a white solid.

Please amend the paragraph at page 443, lines 7-12 to read as follows.

In a manner similar to that in Example 455, by using 5-methylfuran-2-carboxylic acid obtained in ~~Step 3~~ Step 2, in place of isonicotinic acid, followed by reslurrying with ethanol, the entitled Compound 512 (123 mg, 71 %) was obtained as a brown solid from Compound 454 (125 mg, 0.450 mmol).

Please amend the paragraph at page 455, lines 7-15 to read as follows.

Compound 531 (120 mg, 0.300 mmol) was dissolved in THF (2 mL), and a 2 mol/L solution of dimethylamine in THF ~~(0.054 mL, 1.80 mmol)~~ (0.9054 mL, 1.80 mmol) was added thereto, followed by stirring at room temperature for 4.5 hours. The reaction mixture was concentrated under reduced pressure, and the resulting residue was purified through silica gel column chromatography (chloroform), followed by reslurrying with a mixed solvent of 2-propanol and diethyl ether to afford the entitled Compound 533 (64.1 mg, 10 %).

Please amend the paragraph at page 458, lines 4-9 to read as follows.

In a manner similar to that in Example 533, by using (S)-2-methoxymethylpyrrolidine (104 mg, 0.900 mmol) in place of the solution of dimethylamine in THF, followed by reslurrying with a mixed solvent of 2-propanol and hexane, the entitled Compound 538 (92.6 mg, 71 %) was obtained as a white solid from Compound 531 (120 mg, 0.300 mmol).

Please amend the paragraphs at page 472, lines 6-27 to read as follows.

In a manner similar to that in Example 533, by using 1-methylpiperazine ~~(0.100 mL, 9.00 mmol)~~ (0.100 mL, 0.900 mmol) in place of the solution of dimethylamine in THF, followed by recrystallizing from diethyl ether, the entitled Compound 562 (43.4 mg, 35 %) was obtained as a pale orange solid from Compound 531 (120 mg, 0.300 mmol).

^{1}H NMR (DMSO-d_6, δ ppm): 1.40-1.75 (m, 4H), 2.30-2.45 (m, 4H), 3.10-3.22 (m, 1H), 3.33 (s, 3H), 3.34-3.50 (m, 8H), 3.87 (ddd, J = 2.2, 12.1, 12.1 Hz, 2H), 6.69 (dd, J = 1.9, 3.5 Hz, 1H), 7.39 (dd, J = 0.8, 3.5 Hz, 1H), 7.89 (dd, J = 0,8, 1.9 Hz, 1H).

APCIMS m/z: $[M+H]^+$ 419.

m.p.: 106-112°C.

[Example 563]

N-[4-(2-Furyl)-5-(tetrahydropyran-4-ylcarbonyl)thiazol-2-yl]-2-(4-isopropylpiperazin-1-yl)acetamide (Compound 563)

In a manner similar to that in Example 533, by using 1-isopropylpiperazine ~~(115 mg, 9.00 mmol)~~ (115 mg, 0.900 mmol) in place of the solution of dimethylamine in THF, followed by reslurrying with a mixed solvent of ethanol and diethyl ether, the entitled Compound 563 (85.5 mg, 64 %) was obtained as a gray solid from Compound 531 (120 mg, 0.300 mmol).

Please amend the paragraphs starting at page 473, line 26 and ending at page 474, line 19 to read as follows.

In a manner similar to that in Example 533, by using ~~2-hydroxy-2-methylpropylpiperazine~~ 1-(2-hydroxy-2-methylpropyl)piperazine (143 mg, 9.00 mmol) in place of the solution of dimethylamine in THF, followed by reslurrying with a mixed solvent of diisopropyl ether and hexane, the entitled Compound 565 (112 mg, 78 %) was obtained as a pale orange solid from Compound 531 (120 mg, 0.300 mmol).

^{1}H NMR (DMSO-d_6, δ ppm): 1.07 (s, 6H), 1.50-1.80 (m, 4H), 2.48-2.58 (m, 4H), 3.10-3.40 (m, 10H), 3.38 (s, 2H), 3.83-3.92 (m, 2H), 6.69 (dd, J = 1.9, 3.5 Hz, 1H), 7.39 (d, J = 3.5 Hz, 1H), 7.88 (d, J = 1.9 Hz, 1H).

APCIMS m/z: $[M+H]^+$ 477.

m.p.: 106-108°C.

[Example 566]

~~N-[4-(2-Furyl)-5-(tetrahydropyran-4-ylcarbonyl)thiazol-2-yl]-2-[4-(2-hydroxy-2-methylpropyl)piperazin-1-yl]acetamide~~ N-[4-(2-Furyl)-5-(tetrahydropyran-4-ylcarbonyl)thiazol-2-yl]-2-[4-(2-methoxy-2-methylpropyl)piperazin-1-yl]acetamide (Compound 566)

In a manner similar to that in Example 533, by using ~~2-methoxy-2-methylpropylpiperazine~~ 1-(2-methoxy-2-methylpropyl)piperazine (155 mg, 9.00 mmol) in place of the solution of dimethylamine in THF, followed by reslurrying with a mixed solvent of diisopropyl ether and hexane, the entitled Compound 566 (66.5 mg, 45 %) was obtained as a pale orange solid from Compound 531 (120 mg, 0.300 mmol).

Please amend the paragraphs at page 480, lines 4-24 to read as follows.

In a manner similar to that in Example 545, by using ~~1,4-diazepane~~ 1,4-perhydroxazepin hydrochloride (125 mg, 0.900 mmol) in place of 4-methoxypiperidine hydrochloride, followed by reslurrying with diethyl ether, the entitled Compound 575 (83.5 mg, 66 %) was obtained as a white solid from Compound 531 (120 mg, 0.300 mmol).

^{1}H NMR ($CDCl_3$, δ ppm): 1.70-2.00 (m, 6H), 2.86-2.93 (m, 4H), 3.10-3.20 (m, 1H), 3.47 (s, 2H), 3.48 (ddd, J = 2.7, 11.1, 11.1 Hz, 2H), 3.75-3.87 (m, 4H), 4.03 (ddd, J = 2.7, 3.7, 11.1 Hz, 2H), 6.57 (dd, J = 1.9, 3.5 Hz, 1H), 7.59 (d, J = 1.9 Hz, 1H), 7.78 (d, J = 3.5 Hz, 1H).

APCIMS m/z: $[M+H]^+$ 420.

[Example 576]

N-[4-(2-Furyl)-5-(tetrahydropyran-4-ylcarbonyl)thiazol-2-yl]-2-(4-methyl-1,4-diazepan-1-yl)acetamide (Compound 576)

In a manner similar to that in Example 533, by using 1-methyl-1,4-diazepane ~~(143 mg, 9.00 mmol)~~ (143 mg, 0.900 mmol) in place of the solution of dimethylamine in THF, followed by recrystallizing from a mixed solvent of ethanol and diethyl ether, the entitled Compound 576 (50.3 mg, 39 %) was obtained from Compound 531 (120 mg, 0.300 mmol).

Please amend the paragraphs at page 481, lines 5-27 to read as follows.

In a manner similar to that in Example 533, by using 1-adamantylamine ~~(136 mg, 9.00 mmol)~~ (136 mg, 0.900 mmol) in place of the solution of dimethylamine in THF, followed by reslurrying with diethyl ether, the entitled Compound 577 (92.6 mg, 66 %) was obtained as a pale brown solid from Compound 531 (120 mg, 0.300 mmol).

^{1}H NMR (DMSO-d_6, δ ppm): 1.50-1.80 (m, 16H), 2.00-2.05 (m, 3H), 3.10-3.25 (m, 1H), 3.35-3.50 (m, 2H), 3.53 (s, 2H), 3.87 (ddd, J = 2.4, 4.0, 12.1 Hz, 2H), 6.66 (dd, J = 1.6, 3.2 Hz, 1H), 7.33 (dd, J = 0.8, 3.2 Hz, 1H), 7.84 (dd, J = 0.8, 1.6 Hz, 1H).

APCIMS m/z: $[M+H]^+$ 470.

m.p.: 168-170°C.

[Example 578]

N-[4-(2-Furyl)-5-(tetrahydropyran-4-ylcarbonyl)thiazol-2-yl]-2-(3-hydroxyadamantan-1-ylamino)acetamide (Compound 578)

In a manner similar to that in Example 533, by using 1-amino-3-hydroxyadamantane ~~(151 mg, 9.00 mmol)~~ (151 mg, 0.900 mmol) in place of the solution of dimethylamine in THF, followed by reslurrying with diethyl ether, the entitled Compound 578 (102 mg, 70 %) was obtained from Compound 531 (120 mg, 0.300 mmol).

Please amend the paragraph at page 482, lines 7-27 to read as follows.

In a manner similar to that in Example 533, by using imidazole ~~(62.0 mg, 9.00 mmol)~~ (62.0 mg, 0.900 mmol) in place of the solution of dimethylamine in THF, followed by recrystallizing from a mixed solvent of ethanol and diethyl ether, the entitled Compound 579 (43.2 mg, 37 %) was obtained from Compound 531 (120 mg, 0.300 mmol).

^{1}H NMR ($CDCl_3$, δ ppm): 1.70-2.00 (m, 4H), 3.05-3.20 (m, 1H), 3.40-3.50 (m, 2H), 3.90-4.10 (m, 2H), 4.98 (s, 2H), 6.54 (dd, J = 1.6, 3.2 Hz, 1H), 7.07 (s, 1H), 7.18 (s, 1H), 7.53 (d, J = 1.6 Hz, 1H), 7.65 (d, J = 3.2 Hz, 1H), 7.73 (s, 1H).

APCIMS m/z: $[M+H]^+$ 387.

[Example 580]

N-[4-(2-Furyl)-5-(tetrahydropyran-4-ylcarbonyl)thiazol-2-yl]-2-(2-methylimidazol-1-yl)acetamide (Compound 580)

In a manner similar to that in Example 533, by using 2-methylimidazole ~~(74.0 mg, 9.00 mmol)~~ (74.0 mg, 0.900 mmol) in place of the solution of dimethylamine in THF, followed by recrystallizing from a mixed solvent of ethanol and diethyl ether, the entitled Compound 580 (9.1 mg, 8 %) was obtained from Compound 531 (120 mg, 0.300 mmol).

Please amend the paragraphs at page 488, lines 4-8 to read as follows.

^{1}H NMR ($CDCl_3$, δ ppm): 1.88-2.05 (m, 2H), 2.22-2.29 (m, 2H), 2.68-2.84 (m, 4H), 2.94-3.03 (m, 1H), 6.51 (dd, J = 1.8, 3.6 Hz, 1H), 7.48 (dd, J = 0.7, 3.6 Hz, 1H), 7.71-7.48 (m, 3H), 8.85 (d, J = 6.3 Hz, 2H), 10.6 (br s, 1H).

~~APCIMS m/z: [M+H]+ 398~~ APCIMS m/z: $[M+-H]^-$ 398.

Please amend the paragraph at page 508, lines 23-27 to read as follows.

^{1}H NMR ($CDCl_3$, δ ppm): 1.03 (s, 9H), 1.50 (s, 6H), 1.71-1.80 (m, 4H), 1.80 (s, 2H), 3.05 (tt, J = 3.9, 11.2 Hz, 1H), 3.40 ddd, J = 1.6, 11.6, 11.6 Hz, 2H), 3.95-4.10 (m, 2H), ~~5.87 'br s, 1H)~~ 5.87 (br s, 1H), 6.55 (dd, J = 1.8, 3.5 Hz, 1H), 7.45 (d, J = 3.5 Hz, 1H), 7.54 (d, J = 1.8 Hz, 1H).

Please amend the paragraph starting at page 515, line 10 and ending at page 516, line 3 to read as follows.

2-Acetylfuran (5.1 g, 46.0 mmol) was dissolved in a mixed solvent of dichloromethane (50 mL) and methanol (50 mL), and tetra(n-butyl)ammonium bromide (22.3 g, 46.0 mmol) was added thereto, followed by stirring at room temperature for 1 hour. The reaction mixture was concentrated under reduced pressure, water was added to the resulting residue, followed by extraction with ethyl acetate. The organic layer was washed with a saturated aqueous solution of sodium chloride and dried over anhydrous magnesium sulfate, and then the solvent was distilled away under reduced pressure. The resulting residue was dissolved in acetonitrile (60 mL), thiourea (3.5 g, 46.0 mmol) was added thereto, followed by stirring ~~at room temperature~~ under heating and reflux for 30 minutes. The precipitated solid was collected by filtration, and the resulting solid was dissolved in a mixed solvent of a saturated aqueous solution of sodium hydrogencarbonate and ethyl acetate, and subjected to liquid-liquid separation. The organic layer was washed with a saturated aqueous solution of sodium chloride and dried over anhydrous magnesium sulfate, and then the solvent was distilled away under reduced pressure. The resulting residue was purified through silica gel column chromatography (hexane:ethyl acetate = 3:1) to afford 2-amino-4-(2-furyl)thiazole (1.53 g, 20 %).

Please amend the paragraphs starting at page 517, line 12 and ending at page 518, line 2 to read as follows.

Compound g (500 mg, 2.04 mmol) obtained in Reference Example 7 was dissolved in DMF (10 mL), and N-bromosuccinimide (363 mg, 2.04 mmol) was added

thereto, followed by stirring at room temperature for 1 hour. Water was added to the reaction mixture, followed by extraction with ethyl acetate. The organic layer was washed with a saturated aqueous solution of sodium chloride and dried over anhydrous magnesium sulfate, and then the solvent was distilled away under reduced pressure. The resulting residue was purified through silica gel column chromatography (hexane:ethyl acetate = 4:1) to afford the entitled ~~Compound j~~ Compound i (379 mg, 57 %).

^{1}H NMR ($CDCl_3$, δ ppm): 5.16 (br s, 2H), 6.44 (d, J = 3.3 Hz, 1H), 6.91 (d, J = 3.3 Hz, 1H)

[Reference Example 10]

N-[5-Bromo-4-(2-furyl)thiazol-2-yl]pyridine-4-carboxamide (Compound j)

In a manner similar to that in Example 1, by using Compound g (332 mg, 1.36 mmol) obtained in Reference Example 7 in place of Compound a, the entitled ~~Compound k~~ Compound j (382 mg, 81 %) was obtained.

Please amend the paragraph starting at page 518, line 27 and ending at page 519, line 10 to read as follows.

55 % sodium hydride ~~(2.49 g, 0.0570 mmol)~~ (2.49 g, 57.0 mmol) was suspended in DMF (19 mL), and under ice-cooling, 4-methoxybenzyl alcohol ~~(7.12 mL, 0.057 mmol)~~ (7.12 mL, 57.0 mmol) was added thereto, followed by stirring at room temperature for 1 hour. 2-Chloroisonicotinic acid ~~(3.00 g, 0.0190 mmol)~~ (3.00 g, 19.0 mmol) was added to the reaction mixture, followed by stirring at 80°C for 2 hours. The reaction mixture was poured into a mixture of a saturated aqueous solution of sodium chloride (60 mL) and water (60 mL), and 10 % hydrochloric acid was added to the

resulting solution to adjust the pH to 5, followed by stirring under ice-cooling for 1 hour. The precipitated solid was collected by filtration to afford the entitled Compound l (5.26 g, quantitative) as a white solid.

Please amend the paragraph starting at page 522, line 30 and ending at page 523, line 5 to read as follows.

In a manner similar to that in Reference Example 1, by using 2-(2-fluoropyridin-4-yl)-1-(2-furyl)ethanone (6.16 g, 30.0 mmol) obtained according to the method described in WO03/35639, in place of 1-(2-furyl)-2-(4-pyridyl)ethanone, 2-amino-5-(2-fluoropyridin-4-yl)-4-(2-furyl)thiazole (4.86 g, 62 %) was obtained.

Please amend the paragraph starting at page 523, line 27 and ending at page 524, line 2 to read as follows.

In a manner similar to that in Reference Example 1, by using 2-(2-chloropyridin-5-yl)-1-(2-furyl)ethanone (13.8 g, 62.0 mmol) obtained according to the method described in WO03/35639, in place of 1-(2-furyl)-2-(4-pyridyl)ethanone, 2-amino-5-(2-chloropyridin-5-yl)-4-(2-furyl)thiazole (11.6 g, 67 %) was obtained.

Please amend the paragraph starting at page 527, line 24 and ending at page 528, line 13 to read as follows.

2-Acetylfuran (3.30 g, 30.0 mmol) was dissolved in THF (30 mL), and cooled to -78°C. A 1.0 mol/L solution of lithium hexamethyldisilazide in THF (33.3 mL, 33.0 mmol) was added thereto, and heated up to room temperature, and then stirred at

room temperature for 15 minutes. The reaction mixture was cooled to -78°C, and a solution of 1-ethyl-6-oxo-3-(trifluoromethanesulfonyloxy)-1,6-dihydropyridazine (4.08 g, 15.0 mmol) in THF (5 mL) obtained according to the method described in WO03/039451 was added dropwise thereto, followed by stirring at room temperature for 1.5 hours. The reaction mixture was poured into water, followed by extraction with ethyl acetate. The organic layer was washed with a saturated aqueous solution of sodium chloride and dried over anhydrous magnesium sulfate, and then the solvent was distilled away under reduced pressure. The resulting residue was purified through silica gel column chromatography (hexane:ethyl acetate = 1:1) to afford ~~2-(1-ethyl-6-oxo-1,6-dihydro-3-pyridazinyl)-1-(2-furyl)ethanone~~ 2-(1-ethyl-6-oxo-1,6-dihydropyridazin-3-yl)-1-(2-furyl)ethanone (1.01 g, 29 %).

Please amend the paragraph starting at page 531, line 19 and ending at page 532, line 1 to read as follows.

Methyl ~~2-oxo-1,2-dihydropyridinecarboxylate-5-~~ 2-oxo-1,2-dihydropyridine-5-carboxylate (400 mg, 2.61 mmol) obtained in Step 3 was dissolved in DMF (3 mL), and 55 % sodium hydride (125 mg, 2.87 mmol) and ethyl iodide (0.230 mL, 2.87 mmol) were added thereto, followed by stirring at room temperature for 2 hours. Water was added to the reaction mixture, followed by extraction with ethyl acetate. The organic layer was washed with a saturated aqueous solution of sodium chloride and dried over anhydrous magnesium sulfate, and then the solvent was distilled away under reduced pressure. The resulting residue was purified through silica gel column chromatography

(ethyl acetate) to afford methyl 1-ethyl-2-oxo-1,2-dihydropyridine-5-carboxylate (375 mg, 79 %).

Please amend the paragraph at page 535, lines 10-20 to read as follows.

~~2-Methoxy-5-(methoxymethyl)pyridine~~ 2-Methoxy-5-(hidroxymethyl)pyridine (11.6 g, 83.5 mmol) obtained according to the method described in *Tetrahedron Asymmetry*, Vol. 12, p. 1047, 2001 was dissolved in chloroform (160 mL), and manganese dioxide (14.5 g, 167 mmol) was added thereto, followed by stirring under heating and reflux for 1 hour. The reaction mixture was filtered, and the filtrate was concentrated under reduced pressure. The resulting residue was purified through silica gel column chromatography (hexane:ethyl acetate = 3:2) to afford the entitled Compound z (4.32 g, 37 %) as a white solid.

Please amend the paragraphs starting at page 537, line 6 and ending at page 538, line 1 to read as follows.

Ethyl 3-bromofuran-2-carboxylate (307 mg, 1.40 mmol) obtained in Step 1, phenylboronic acid (208 mg, 1.71 mmol), dichlorobis(tri-O-tolylphosphine)palladium(II) (60.3 mg, 0.008 mmol) and potassium carbonate (387 mg, 2.80 mmol) were dissolved in a mixed solvent of toluene (13 mL), ethanol (0.65 mL) and water (1.4 mL), followed by stirring at 90°C for 6 hours. Aqueous saturated sodium hydrogencarbonate solution was added to the reaction mixture, followed by extraction with ethyl acetate. The organic layer was washed with a saturated aqueous solution of sodium chloride and dried over

anhydrous magnesium sulfate, and then the solvent was distilled away under reduced pressure. The resulting residue was purified through silica gel column chromatography (hexane:ethyl acetate = 6:6) to afford ~~ethyl 3-phenyl-2-carboxylate~~ ethyl 3-phenylfuran-2-carboxylate (290 mg, 96 %).

^{1}H NMR ($CDCl_3$, δ ppm): 1.30 (t, J = 7.3 Hz, 3H), 4.31 (q, J = 7.3 Hz, 2H), 6.61-6.62 (m, 1H), 7.35-7.44 (m, 3H), 7.54-7.60 (m, 3H).

Step 3:

In a manner similar to that in Reference Example 13, by using 4-methylpyridine in place of 3,4-dimethylpyridine and using ethyl ~~3-phenyl-2-carboxylate~~ 3-phenylfuran-2-carboxylate (277 mg, 1.28 mmol) obtained in Step 2 in place of ethyl furan-2-carboxylate, 2-(3-phenylfuran-2-yl)-1-(4-pyridyl)ethanone (230 mg, 75 %) was obtained.

Please amend the paragraph at page 539, lines 19-22 to read as follows.

In a manner similar to that in Reference Example 13, by using 4-methylpyridine in place of 3,4-dimethylpyridine, the entitled Compound ae (216 mg, 25 %) was obtained from ~~ethyl 3-furan-2-carboxylate~~ ethyl furan-3-carboxylate (502 mg, 3.58 mmol).